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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,088	01/14/2002	Howard A. Fields	14114.0342U2	6001

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Gwendolyn D Spratt
Needle & Rosenberg
Suite 1200
127 Peachtree Street NE
Atlanta, GA 30303-1811

EXAMINER
WORTMAN, DONNA C

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,088	FIELDS ET AL.	
	Examiner	Art Unit	
	Donna C. Wortman, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,15-17,33-37,39,40,42 and 44-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-47* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claims 44-47 were added in Paper No. 8 filed March 31, 2003. As a result, claims 1-47 are pending and subject to restriction as follows.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Groups 1-10, claims 1-5 and 33-47, insofar as drawn to a single peptide having HAV VP4-VP2 epitopes and selected from SEQ ID NO's 1-10, and use of the peptide in immunoassays.

Groups 11-22, claims 1, 2, 6-8, and 33-47, insofar as drawn to a single peptide having HAV VP3 epitopes and selected from SEQ ID NO's 11-22, and use of the peptide in immunoassays.

Groups 23-38, claims 1, 2, 9-11, 33-37, 39, 40, 42 and 43-47 insofar as drawn to a single peptide having HAV VP1 epitopes and selected from SEQ ID NO's 23-38, and use of the peptide in immunoassays.

Groups 39-48, claims 1, 2, 12-14 and 33-47, insofar as drawn to a single peptide having HAV P2A epitopes and selected from SEQ ID NO's 39-48, and use of the peptide in immunoassays.

Group 49, claims 1, 2, 15-17, 33-37, 39, 40, 42, and 44-47, insofar as drawn to a single peptide having HAV P2B epitopes, SEQ ID NO:49, and use of the peptide in immunoassays.

Groups 50-61, claims 1, 2, 18-20, 33-37, 39, 40, 42 and 44-47, insofar as drawn to a single peptide having HAV P2C epitopes and selected from SEQ ID NO's 50-61, and use of the peptide in immunoassays.

Groups 62-65, claims 1, 2, 21-23, 33-37, 39, 40, 42 and 44-47, insofar as drawn to a single peptide having HAV P3A epitopes and selected from SEQ ID NO's 62-65, and use of the peptide in immunoassays.

Group 66, claims 1, 2, 24-26, 33-37, 39, 40, 42 and 44-47, insofar as drawn to a single peptide having HAV P3B epitopes, SEQ ID NO:66, and use of the peptide in immunoassays.

Groups 67-72, claims 1, 2, 27-29, and 33-47, insofar as drawn to a single peptide having HAV P3C epitopes and selected from SEQ ID NO's 67-72, and use of the peptide in immunoassays.

Groups 73-88, claims 1, 2, and 30-47, insofar as drawn to a single peptide having HAV P3D epitopes and selected from SEQ ID NO's 73-88, and use of the peptide in immunoassays.

The inventions listed as Groups I-88 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

A national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention "). Where a group of inventions is claimed in an application, the requirement of unity of invention is fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" means those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. In this regard, WO 97/40147, listed on PTO 1449 filed November 18, 2002 as Paper No. 6, is cited as anticipating at least independent claim 1, since WO 97/40147 discloses several antigenic HAV peptides with one or more glutamine residues at the carboxyl end of the peptide: see, e.g., WO 97/40147, SEQ ID NO's 7, 8, 12, 16, 46, 48, 61, 65, 66, and 72. Consequently, the claimed inventions 1-88 as listed above cannot be said to share a

special technical feature, and the election of a single invention, i.e., a single peptide, is required.

Applicant's election with traverse of Group 49, SEQ ID NO:49, in Paper No. 8 is acknowledged. The traversal is on the ground(s) that the newly added claims 44-47 render the restriction requirement moot because the newly added claims recite the same special technical feature, viz., a non-native glutamine residue that provide an increase in antigenic/immunological reactivity not suggested in the art, and that all the claimed subject matter of claims 44-47 should be examined as a single group. Applicant has asserted that no serious burden has been shown if all of the claims are examined together. Alternatively, Applicant has requested that at least ten sequences be examined, and has provisionally elected claims 44-47 as drawn to SEQ ID NOs 39-45, 47, and 49. As a final alternative, Applicant elects SEQ ID NO:49. Applicant's traversal is not found persuasive because claims 1-43, which encompass all of the SEQ ID NO's recited in claims 44-47, as well as additional SEQ ID NO's, remain pending. Claims 44-47 merely recite a subset of the peptides previously, and still, claimed. The entire set of claims lacks unity of invention as not sharing a common technical feature for the reasons given in Paper No. 7 and repeated above. Further, since each peptide claimed requires a separate sequence and database search and separate consideration, examining more than one peptide would constitute a serious burden on the Office.

The requirement is still deemed proper and is therefore made FINAL.

Consequently, claims 1, 2, 15-17, 33-37, 39, 40, 42, and 44-47, insofar as drawn to SEQ ID NO:49, are under examination. Claims 3-14, 18-32, 38, 41, and 43, and the portions of claims 1, 2, 34, 37, 40, 42, and 44-47 that do not read on SEQ ID NO:49 are withdrawn from consideration as drawn to non-elected inventions.

Claims 1, 2, 34, 37, 40, 42, and 44-47 are objected to because of the following informalities: Claims 1, 2, 34, 37, 40, 42, and 44-47 recite non-elected subject matter.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 15-17, 33-37, 39, 40, 42, and 44-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide immunoreactive with HAV antibodies, wherein the peptide comprises or consists of the amino acid sequence of SEQ ID NO: 49, and immunoassays using that peptide, does not reasonably provide enablement for a peptide comprising or consisting of SEQ ID NO:49 with more than one glutamine residue at the carboxyl terminal end of the peptide, nor for a peptide comprising or consisting of conservative variations of a peptide comprising or consisting of the amino acid of SEQ ID NO:49. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims encompass peptides made by adding an unlimited number of glutamine residues to the carboxyl terminal end of SEQ ID NO:49 as well as peptides made by substituting an unlimited number of amino acids with amino acids that are considered conservative

variants. The specification describes how to make and use only peptides that have a single glutamine at the carboxyl terminus and, while it states that "conservative substitutions" means substituting amino acids that are "biologically and/or chemically similar" and lists substitutions that are chemically similar (specification, page 34, line 24-page 35, line 7), it does not teach which of the chemically similar substitutions would result in biologically (in this context, antigenically or immunogenically) similar peptides. WO 97/40147 teaches the difficulty in designing synthetic peptides for use in immunoassays for HAV antibodies because HAV antigenic epitopes are "strictly conformational" in nature (WO 97/40147, page 1, lines 24-29); further, WO 97/40147 shows that the reactivity of overlapping peptides with HAV sera varies considerably and can only be demonstrated empirically (see, e.g., WO 97/40147, the tables on pages 49-56). The antigenic or immunogenic effect of adding additional glutamine residues or of substituting chemically similar amino acids to peptides of demonstrated HAV antigenic reactivity is therefore unpredictable. Considering the breadth of the claims, the amount of guidance presented in the specification, the state of the art, and the unpredictability in designing synthetic HAV peptides that are immunoreactive with HAV antibodies in patient sera, the specification does not enable one of skill in the art to practice the invention throughout the scope of the claims without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 33, 36, 39 and 43 are all indefinite because the language in the preamble does not correlate with the results actually obtained in the final, "detecting," step.

Claim 33 recites "A method of detecting the presence of Hepatitis A virus" but recites steps that result in detecting binding of peptide with antibody in a sample. No steps recite or result in actually detecting any virus.

Claim 36 recites "A method for detecting the presence of antibodies against ... HAV" but correlates the presence of antibodies with the presence of virus although the method is not recited to be a method for detecting virus and no steps for detection of virus are recited.

Claim 39 recites "A method for detecting acute phase infection" and recites that "detection of IgM antibodies indicates the presence of HAV." No steps for detection of virus are recited, and no language correlates with detection of acute phase infection.

Claim 40 recites "A method for detecting convalescence in a mammal" and recites, as a final step, "detecting total antibody titer by measuring binding to immunogenic peptides." There are no steps for detecting convalescence and no language that serves to relate particular antibody titers with convalescence.

Applicant is cautioned against the introduction of new matter in amending the claims.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 33, 34, 35, 36, 37, 39, 40, 42 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Fields et al., WO 97/40147, of record. Fields et al. disclose a number of synthetic peptides that are immunoreactive with HAV antibodies and that have one or more glutamines at the carboxyl terminal and their use in immunoassays. See, e.g., Fields et al., SEQ ID NO's 7, 8, 12, 16, 46, 48, 61, 65, 66, 71, and 72 (listed, e.g., on pages 9-11). Fields teaches making conservative substitutions of amino acids in the peptides (page 22, line 25-page 23, line 21); labeling the peptides (page 27, lines 27-35, e.g.); and immunoassays using the peptides (page 36, line 10-page 37, line 25, e.g.).

SEQ ID NO:49 is free of the prior art. While the prior art teaches a peptide consisting of amino acids 1-20 of SEQ ID NO:49 (see SEQ ID NO:49 of Fields, WO 97/40147), it does not teach or fairly suggest the addition of a glutamine at the carboxyl end of that peptide. Claims limited to a peptide comprising or consisting of the amino acid sequence of SEQ ID NO:49 and its use in immunoassays would be allowable assuming that all such claims comply with 35 USC 112, first and second paragraphs.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna C. Wortman, Ph.D. whose telephone number is

703-308-1032. The examiner can normally be reached on Monday-Thursday, 7:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Donna C. Wortman, Ph.D.
Primary Examiner
Art Unit 1648

dcw
June 13, 2003